

Human skin resident T cells in health and disease

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One of the most exciting recent discoveries in T cell immunobiology is the discovery of non-recirculating resident memory cells (T_{RM}). These cells remain long-term in peripheral tissues and provide frontline protection against infections. The healthy skin surface of a healthy adult contains 20 billion memory T cells, nearly twice as many as are present in the entire circulation. Approximately 80% of these cells are nonrecirculating T_{RM} . These cells are critically important in defending against infection but when they become autoreactive or malignant, they give rise to dermatologic diseases such as psoriasis and mycosis fungoides (MF), respectively. The antigen specificity of T_{RM} in human gut, lung and skin are largely nonoverlapping and are enriched for organisms encountered through that particular barrier tissue. We find also that human skin cancers, including squamous cell carcinoma, Merkel cell carcinoma and melanoma have evolved mechanisms to either exclude or inactivate skin T_{RM} . Lastly, we find that MF and Sézary syndrome, two subtypes of cutaneous T-cell lymphoma (CTCL), are derived from distinct T-cell subsets. MF has markers suggesting it derives from nonrecirculating, sessile T_{RM} . This is consistent with the tendency of inflammatory plaques to remain fixed for many years and to recur after cessation of therapy. In contrast, L-CTCL derives from central memory T cells, a type of T cell that actively recirculates between the blood skin and lymph nodes. In response, we have begun to use therapies that selectively deplete T_{RM} vs. T_{CM} to selectively kill malignant cells while sparing benign T cells.